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1/28/09 Michelle Hobson
Date Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Examiner: J. Woitach
CHOO et al.	Group Art Unit: 1636
Serial No.: 09/996,484	Confirmation No.: 2713
Filing Date: November 28, 2001	Customer No.: 20855
Title: MOLECULAR SWITCHES	

BRIEF ON APPEAL UNDER 37 C.F.R. § 41.37

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Appeal Brief is filed pursuant to 37 C.F.R. § 41.37 (see, Fed. Reg. vol. 73. no. 238, page 74972 published December 10, 2008) and is in response to the Final Office Action mailed on June 4, 2008. A Notice of Appeal was received on December 4, 2008, making an Appeal Brief initially due on or before February 4, 2009. Accordingly, this Brief is timely filed.

REAL PARTY IN INTEREST

Gendaq Ltd. is the assignee of the instant application, as recorded on August 22, 2005 in the USPTO at Reel 016655, Frame 0867. See, also, Certificate Under 37 C.F.R. § 3.73(b) filed on April 1, 2002. Gendaq, Ltd. is a wholly owned subsidiary of Sangamo BioSciences, Inc. Therefore, the real party in interest is Sangamo BioSciences, Inc.

RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any related appeals or interferences.

STATUS OF CLAIMS

Pending: Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 34, 35 and 38-48

Canceled: Claims 3, 6, 9, 12, 16-20, 27-30, 32, 33, 36, 37, 49

Withdrawn: Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 35 and 38-47

Appealed: Claims 34 and 48

STATUS OF AMENDMENTS

No amendments have been made subsequent to the mailing of the Final Office Action on June 4, 2008.

Appellants note that their Response after Final was mailed within 2 months of the mailing of the Final Office Action and, therefore, expedited procedure was in order. However, no Advisory Action was ever received, despite repeated telephone calls and a written status inquiry to the Office.

SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 34 is drawn to a complex (page 10, lines 16-19) comprising (a) a heterodimer comprising first and second polypeptides (page 2, lines 8-11) and (b) a ligand (page 10, lines 18-19). The ligand binds to the first and second polypeptides and mediates heterodimerization of these two polypeptides (page 49, line 25; page 58, lines 12-14; page 59, lines 4-5; paragraph bridging pages 54-55). The first and second polypeptides bind to

DNA, and, in addition, the first or second polypeptide comprises an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain (page 23, line 4 through page 31, line 31).

Independent claim 48 is drawn to a switching system comprising a protein switch (page 5, lines 14-15) comprising: (i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide (page 5, lines 15-16), in which the first polypeptide binds to the second polypeptide and the binding of the polypeptides is mediated by a ligand and that binds to both polypeptides (page 5, line 14), and (iii) a third component comprising the ligand, wherein the first and second polypeptides bind to DNA (page 5, lines 18-20), and further wherein the first or second polypeptide comprises an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain (page 23, line 4 through page 31, line 31).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Whether claims 34 and 48 are unpatentable under 35 U.S.C. § 112, 1st paragraph as not adequately described by the as-filed specification.

B. Whether claims 34 and 48 are unpatentable under 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite.

C. Whether claims 34 and 48 are unpatentable under 35 U.S.C. § 103(a) as obvious in view of WO 96/06110 (hereinafter "Gilman").

ARGUMENTS

A. Claims 34 and 48 are fully described by the as-filed specification

Claims 34 and 48 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement by containing subject matter that was not described in the originally-filed specification. (Final Office Action, pages 3-4). In particular, it was alleged that the recitation "non-naturally occurring" was not adequately described because naturally occurring DNA binding domains may mutate. *Id.*

For the reasons of record, Appellants reiterate that that the term "non-naturally occurring" is amply described in the as-filed specification. It is well settled that the written description requirement is satisfied if the specification reasonably conveys possession of the invention to one skilled in the art. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). The disclosure must be read in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981). Moreover, the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976).

In the case on appeal, the rejection is premised on the assertion that non-naturally occurring is not adequately described because naturally occurring DNA binding domains can "mutate" spontaneously. (Final Office Action, pages 3-4). However, no evidence is given by the Examiner in support of this assertion, and spontaneous mutations in the binding region of these proteins has not been documented. The line of reasoning followed by the Examiner is completely nonsensical. Following this thinking, patents should never be granted for any novel protein or chemical structure, because there may be a chance that somewhere, in some unknown organism, the novel compound may already have been made, "as a consequence of continual mutation."

Moreover, the basis of the rejection, namely that naturally occurring zinc finger proteins may mutate spontaneously, is utterly irrelevant to a written description inquiry – an

applicant is not required to present a list of all non-naturally occurring (or all naturally occurring) Cys2-His2 zinc finger proteins in order to satisfy the written description requirement of claims directed to "non-naturally occurring" Cys2-His2 zinc finger proteins. Rather, what is required is that an applicant demonstrates possession of the claimed subject matter. Here, the as-filed specification contains ample description of both naturally and non-naturally occurring Cys2-His2 zinc finger DNA binding domains (see, e.g., paragraphs [0107] and [0120], emphasis added):

> A zinc finger binding motif is a structure well known to those in the art and defined in, for example. Miller et al., (1985) EMBO J. 4:1609-1614; Berg (1988) PNAS (USA) 85:99-102: Lee et al. (1989) Science 245:635-637; see International patent applications WO 96/06166 and WO 96/32475, corresponding to U.S. Ser. No. 08/422.107, incorporated herein by reference.
>
> In general, naturally occurring zinc fingers may be selected from those fingers for which the DNA binding specificity is known. For example, these may be the fingers for which a crystal structure has been resolved: namely Zif 268 (Elrod-Erickson et a!., (1996) Structure 4:1171-1180), GLI (Pavletich and Pabo, (1993) Science 261:1701-1707), Tramtrack (Fairall et al., (1993) Nature 366:483 487) and YYI (Houbaviv et al., (1996) PNAS (USA) 93:13S77-13582).

The as-filed specification also clearly describes that non-naturally occurring zinc finger proteins as claimed were known to be obtainable by design or selection at the time of filing (paragraphs [0009], [0039], [0119], [0122], and [0125], emphasis added):

> Preferably, at least one of the candidate first molecules comprises a non-naturally occurring binding domain which binds to the second molecule. The term "a non-naturally occurring binding domain" means that the binding domain does not occur in nature, even as part of a larger molecule, and has been obtained by deliberate mutagenesis procedures or de novo design techniques. **94:**5525-5530; and Beerli *et al.* (1998) *Proc. Natl. Acad. Sci. USA* **95:**14628-14633.
>
> As used herein the terms "peptide", "polypeptide" and "protein" refer to a polymer in which the monomers are amino acids and are joined together through peptide or disulfide bonds. "Polypeptide" refers to either a full-length

naturally-occurring amino acid chain or a "fragment thereof" or "peptide", such as a selected region of the polypeptide that binds to another protein, peptide or polypeptide in a manner modulatable by a ligand, or to an amino acid polymer, or a fragment or peptide thereof, **which is partially or wholly non-natural**.

We also describe a method for preparing a DNA binding protein of the Cys2-His2 zinc finger class capable of binding to a target DNA sequence in a manner modulatable by a ligand, comprising the steps of: (a) selecting a model zinc finger domain from the group consisting of naturally occurring zinc fingers and consensus zinc fingers: and (b) mutating at least one of positions -1, +3, +6 (and ++2) of the finger as required by a method according to the present invention.

The naturally occurring zinc finger 2 in Zif 268 makes an excellent starting point from which to engineer a zinc finger and is preferred.

When the nucleic acid specificity of the model finger selected is known, the mutation of the finger in order to modify its specificity to bind to the target DNA may be directed to residues known to affect binding to bases at which the natural and desired targets differ. Otherwise, mutation of the model fingers should be concentrated upon residues -1, +3, +6 and ++2 as provided for in the foregoing rules.

Furthermore, the specification need not describe, and preferably omits, that which is well known to the skilled artisan. At the time of filing, the skilled artisan was well that the term non-naturally occurring clearly refers to those Cys2-His2 zinc finger DNA binding domains that had been engineered (e.g., by design, selection or mutagenesis) to bind to a selected target site. See, e.g., Refs. B13 and B16 of the IDS mailed on October 24, 2003 and cited, along with other references regarding engineering of non-naturally occurring Cys2-His2 zinc finger binding domains on paragraph [0085] of the as-filed specification.

Thus, the skilled artisan would have no doubt that the as-filed specification, in light of the state of the art at the time of filing, describes non-naturally occurring zinc finger proteins as those that do not occur in nature. Furthermore, the Office has not identified any Cys2-His2 zinc finger DNA binding domains having random, naturally occurring mutations and,

even if such proteins exist, they are not encompassed by the claims because they would be naturally occurring.

Appellants also note that the Board of Patent Appeals and Interferences has recently reaffirmed that the term "naturally occurring" would be understood by the persons of skill in the art to mean that it exists or is found in nature. *See,* page 3 of *Ex parte Dewis et al.* (2007) Appeal 2007-1610 (BPAI), attached hereto. Plainly, the skilled artisan would know that "non-naturally occurring" refers to zinc finger proteins that do not exist or are found in nature.

Since it is clear that the skilled artisan would have known that Appellants were in possession of non-naturally occurring Cys2-His2 zinc finger proteins as claimed, namely by engineering via design or selection to produce a zinc finger protein that does not occur in nature, withdrawal of the rejection is in order.

B. Claims 34 and 48 are clear and definite

Claims 34 and 48 were also rejected under 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite for reciting a "non-naturally occurring Cys2-His2 zinc finger binding domain." (Final Office Action, pages 4-5).

As detailed in their Response After Final, Appellants traversed the rejection, noting that the term "non-naturally occurring Cys2-His2 zinc finger binding domain" is completely clear to the skilled artisan.

The definiteness requirement of 35 U.S.C. § 112, second paragraph is satisfied if it is clear to the skilled artisan what is meant by a particular claim term. *See, e.g., In re Marosi,* 218 USPQ 289 (Fed. Cir. 1983). The definiteness and clarity of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular disclosure; (2) the teachings of the art; and (3) the claim interpretation that would be given by one possessing ordinary skill in the pertinent art at the time the invention was made. *See, e.g., W.L. Gore & Assocs., Inc. v. Garlock, Inc.,* 220 USPQ 202 (Fed. Cir. 1983).

In the case on appeal, the as-filed specification more than clearly defines what is encompassed by the recitation "non-naturally occurring" Cys2-His2 zinc finger protein.

Specifically, as discussed in the record and the instant Brief, the term "non-naturally occurring" clearly refers to any binding domain that does not occur in nature, namely zinc finger proteins which have been altered in the recognition region helix by design or selection to bind to a selected target site. See, also citations from the specification above in Section A regarding 35 U.S.C. § 112, 1st paragraph.

Thus, it is clear from the as-filed specification that the term "non-naturally occurring" refers to a zinc finger protein in which the DNA recognition regions of one or more of the component fingers have been designed or selected for binding to a particular target site.

Finally, the Examiner's assertion that it is "impossible" to know whether any sequence is naturally occurring because not all naturally occurring proteins are known and because proteins change over time is incorrect and does not support the contention that the claims are indefinite. Zinc finger proteins can be naturally-occurring or they can be non-naturally-occurring; the claims make explicit that the claimed zinc finger DNA-binding domain is non-naturally-occurring. Furthermore, at any point in time, through ordinary searching of the extensive databases now available publically to the artisan, it is a simple and straightforward matter for one of skill in the art to determine what is or is not naturally-occurring; thereby determining what is encompassed by the claims.

Thus, in view of the specification as a whole and state of the art, the claims are clear and withdrawal of the rejection is in order.

C. Claims 34 and 48 are non-obvious over Gilman

Claims 34 and 48 were rejected as allegedly obvious over WO 96/06110 (hereinafter "Gilman"). (Final Office Action, pages 5-9). Gilman was cited for allegedly teaching all the claimed elements except for a non-naturally occurring Cys2-His2 zinc finger binding domain, although "non-naturally occurring" was alleged to be "impossible" to determine and/or encompassed by Gilman's disclosure of phage display libraries. *Id.*

Again, the rejection cannot be sustained if the term "non-naturally occurring" as applied to Cys2-His2 zinc finger domain is properly interpreted in the context of the claim. For the reasons detailed above, it is entirely clear and definite what is encompassed by the

recitation "non-naturally occurring." The specification in fact clearly defines what is meant by the claim term.

Moreover, as set forth in *Philips v. AWH*, 75 USPQ2d, 1321, 1326 (Fed. Cir. 2005) (and a host of prior case law[1]) the primary determinant of the meaning of a claim term is the ordinary and customary meaning of that term:

> the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention.

The ordinary and customary meaning of the term "non-naturally occurring" is something that does not occur naturally, for example Cys2-His2 zinc finger proteins whose recognition domains had been designed and/or selected (engineered) to bind to a target site of choice. As noted above, evidence has also been provided establishing that the Board considers the ordinary and customary meaning of the term "non-naturally occurring" to be any composition that does not occur in nature. See, *Ex parte Dewis,* Evidence Appendix (1). Further, nothing in the specification contradicts what one of ordinary skill in the art of Cys2-His2 zinc fingers, as of Appellants' filing date, would consider to be the ordinary and customary meaning of the term "non-naturally occurring."

The pending claims require that the DNA binding domain be non-naturally occurring and, thus, every naturally occurring DNA binding domain sequence is excluded from the scope of the claims. Thus, as acknowledged Gilman fails to teach or suggest anything about engineered zinc finger proteins in addition to failing to teaching anything about non-naturally occurring Cys2-His2 zinc finger binding domains.

Importantly, Gilman also fails to teach, suggest or enable complexes as claimed in which heterodimerization of first and second DNA binding domains is mediated by a ligand that binds to the DNA binding domains. Rather, Gilman teaches that DNA binding domains

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[1] See, e.g., *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576 (Fed. Cir. 1996); *Ferguson Beauregard/Logic Controls v. Mega Sys., LLC*, 350 F.3d 1327, 1338 (Fed. Cir. 2003); *Innova Pure Water, Inc. v. Safari Water Filtration Systems, Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004) and *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004)

are either covalently linked (i.e., via a linker in a fusion protein) (Gilman, page 9) or that fusion proteins containing both a DNA-binding domain and immunophilin ligand-binding domains are linked by a linker that binds to the fused immunophilin domain. Specifically, Gilman discloses that two or more DNA-binding domains are covalently linked via traditional linkers to form a fusion protein. See, Gilman, sections 3 and 4, beginning on page 6 of the disclosure, particularly page 9. Indeed, as previously noted, Gilman clearly links his DNA-binding domains covalently to form "chimeric" or "composite" DNA binding domains. Once covalently linked, a ligand-binding domain may be added an "additional domain" to link two or more composite molecules (page 7, lines 29-36; page 10, lines 17-21; and page 10, lines 22, emphasis added):

> The chimeric proteins may also include a ligand-binding domain to provide for regulatable interaction of the protein with a second polypeptide chain. Thus, in embodiments involving covalently linked composite DNA binding domains, the unitary composite DNA-binding protein may further contain a ligand-binding domain. In such cases, the presence of a ligand-binding domain permits association of the composite DBP, in the presence of a dimerizing ligand, with a second chimeric protein containing a transcriptional activation domain and another ligand-binding domain.
>
> Additional domains, described in the previous section (e.g., activation domains, ligand-binding domains) may be appended to either the N- or C-termini of the DNA-binding domains in any order consistent with the proper functioning of the protein

Gilman also only exemplifies complexes in which two DNA-binding domains are covalently linked as a fusion protein. See, Examples of Gilman. This is entirely unlike the claimed complexes in which a ligand modulates formation of a heterodimer.

Moreover, in terms of ligand-mediated multimerization, Gilman also teaches only that this is accomplished by fusing an immunophilin ligand-binding domain to the DNA-binding domain (page 11, lines 1-22 of Gilman, emphasis added):

> In embodiments involving composite DNA-binding proteins formed by ligand-mediated multimerization rather than by covalent linkage, DNA

> sequences encoding a DNA-binding domain, with any introduced sequence alterations, is joined to DNA encoding one or more suitably engineered ligand-binding domains, and if desired, to DNA encoding a transcriptional activation domain or other optional domain(s). These sequences are joined such that they constitute a single open reading frame that can be translated in cells into a single polypeptide harboring all component domains. The order and arrangement of the domains within the polypeptide can vary. At least two such chimeras are required for the optimal embodiment of this method. These constructions encode polypeptides containing distinct DNA-binding domains, ligand-binding domains with distinct specificity for multimerizing moieties, and in some embodiments, transcriptional activation domains with different properties. For example, this invention includes chimeras of the following structure:
>
> (immunophilin) --- (txn activator) -- (DNA binding domain)
>
> wherein "immunophilin" represents 1, 2 or 3 immunophilin domains, such as the FKBP12 domain of Spencer et al, "txn activator" represents a VP16 domain and "DNA binding domain" represents a DNA binding domain of Phoxl or SRE-ZBP.

As such, Gilman does not teach or suggest the claimed complexes in which the ligand mediates heterodimerization by binding to the DNA-binding polypeptide.

It is well-established that in order to be available as a reference under 35 U.S.C. § 102/103, the reference must contain an enabling disclosure. *See, e.g., Chester v. Miller,* 906 F.2d at 1576 n.2, 15 USPQ2d at 1336 n.2 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner,* 778 F.2d at 781, 227 USPQ at 778 (Fed. Cir. 1985); *Scripps Clinic & Research Found. v. Genentech, Inc.,* 927 F.2d 1565, 1578, 18 USPQ2d 1001, 1011 (Fed. Cir. 1991); *Helifix Ltd. v. Blok-Lok Ltd.,* 208 F.3d 1339, 54 USPQ2d 1299 (Fed. Cir. 2000). In other words, the reference must "sufficiently describe the claimed invention to have placed the public in possession of it." See, *Minnesota Mining & Mfg. Co. ("3M") v. Johnson & Johnson Orthopaedics, Inc.,* 976 F.2d 1559, 1572, 24 USPQ2d 1321, 1332 (Fed. Cir. 1992); see also *In re Donohue,* 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985).

In the instant case, Gilman does not place the public in possession of ligand-mediated heterodimeric complexes as claimed. As noted throughout prosecution and above, Gilman discloses only complexes in which DNA-binding domains are covalently linked or in which

additional immunophilin ligand-binding domains are fused to the DNA-binding domain to mediate dimerization. This is in stark contrast to the claimed complexes in which the ligand mediates heterodimerization by binding to the DNA-binding domains. See, e.g., Example 1.3 on page 89 of the as-filed specification. The fact that the present applicants subsequently demonstrated complexes as claimed cannot be used to supplement the reference.

When taken as a whole, Gilman does not describe, demonstrate or in any way suggest complexes as claimed in claims 34 and 48. Since this reference does not place the public in possession of the complexes comprising a non-naturally occurring Cys2-His2 zinc finger protein bound via a ligand to a second DNA-binding domain, withdrawal of this rejection is in order.

CONCLUSION

For the reasons stated above, Appellants respectfully submit that the pending claims are novel and non-obvious. Accordingly, Appellants request that the rejections of the claims on appeal be reversed, and that the application be remanded to the Examiner so that the appealed claims can proceed to allowance.

Respectfully submitted,

Date: January 28, 2009

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CLAIMS APPENDIX

The claims on appeal are as follows:

34. A complex comprising:

(a) a heterodimer comprising

(i) a first polypeptide, and

(ii) a second polypeptide; and

(b) a ligand that binds to the first and second polypeptides and mediates heterodimerization of the first and second polypeptides,

wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain.

48. A switching system comprising a protein switch comprising: (i) a first component comprising a first polypeptide and (ii) a second component comprising a second polypeptide, in which the first polypeptide binds to the second polypeptide, wherein binding of the first polypeptide to the second polypeptide forms a heterodimer and the binding of the first and second polypeptides is mediated by binding of a ligand to the first and second polypeptides, and (iii) a third component comprising the ligand, wherein the first and second polypeptides bind to DNA, and further wherein the first or second polypeptide comprises an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain.

EVIDENCE APPENDIX

The following document is attached to this Brief:

(1) a copy of *Ex parte Dewis* (2007) Appeal 2007-1610 (BPAI). This case was cited in the Response After Final mailed August 4, 2008. Expedited procedure was in order but an Advisory Action indicating consideration of this document was never received.

RELATED PROCEEDINGS APPENDIX

As noted above on page 2 of this Appeal Brief, Applicants are not aware of any related, currently pending appeals or interferences. Accordingly, no documents are submitted with this Appendix.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte MARK LAWRENCE DEWIS,
DAVID JOHN EDWARDS, LESLEY KENDRICK,
MARIA WRIGHT, and AMIR YUSUF

Appeal 2007-1610
Application 10/955,833
Technology Center 1600

Decided: September 4, 2007

Before TONI R. SCHEINER, LORA M. GREEN, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 7-12. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF CASE

A problem with developing flavoring agents for fruity and herbaceous materials, such as mango flavor, is that natural plant materials do not contain a single flavoring agent, but rather contain a complex mixture of volatile components making identification of characteristic flavors very difficult.

> The volatiles of mango were analyzed by gas chromatography and a combined gas chromatograph-mass spectrometer. The volatiles were also analyzed by gas chromatography on a sulfur detector.

(Spec. 2: 21-27).

The Specification describes the discovery that ethyl 3-mercaptobutyrate – identified from mango – can be used as a flavoring and perfuming agent because of its unique flavor and odorant properties (Spec. 1-2). The claims are drawn to an ingestible composition comprising an ingestible vehicle and ethyl 3-mercaptobutyrate.

The following rejections are on appeal in this proceeding:

1) Claims 7-12 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Answer 13);

2) Claims 7-12 stand rejected (three separate rejections: of claims 7-12, 10-12, and 7; Answer 7, 9, and 13, respectively) under 35 U.S.C. § 112, second paragraph, as indefinite;

3) Claims 7-9 stand rejected under 35 U.S.C. § 102 as anticipated by Nielsen ("Stereoselective Reduction of Thiocarbonyl Compounds with Baker's Yeast," *Tetrahedron: Asymmetry*, 5: 403-410, 1994; referred to by the Examiner as "Nielson and Madsen") (Answer 11); and

4) Claim 7 stands rejected under 35 U.S.C. § 102(b) as anticipated by Lazier (US 2,402,639, issued Jun. 25, 1946; referred to by the Examiner as "Lazier and Signaigo") (Answer 12).

The claims in each rejection stand or fall together because separate reasons for patentability were not provided for any individual claim. We select claims 7 and 10 as representative for deciding all rejections in this appeal. *See* 37 C.F.R. § 41.37(c)(1)(vii). Claims 7 and 10 read as follows:

7. An ingestible composition comprising:
(i) an ingestible vehicle; and
(ii) an organoleptically effective amount of ethyl 3-mercaptobutyrate represented by the formula, $CH_3(SH)CHCH_2COOCH_2CH_3$ provided that the ethyl 3-mercaptobutyrate is not part of a naturally occurring mixture of compounds or part of a synthetic mixture of compounds which is the same as the naturally occurring mixture of compounds.

10. The ingestible composition according to claim 7, wherein the ingestible composition is a beverage product.

CLAIM INTERPRETATION

Claim 7 is drawn to an ingestible composition comprising (i) an ingestible vehicle and (ii) ethyl 3-mercaptobutyrate "provided that the ethyl 3-mercaptobutyrate is not part of a naturally occurring mixture of compounds or a part of a synthetic mixture of compounds which is the same as the naturally occurring mixture of compounds."

At issue in this appeal is the proper interpretation of "provided that the ethyl 3-mercaptobutyrate is not part of a naturally occurring mixture of compounds." We give the words in a claim their broadest reasonable interpretation as they would be understood by persons of skill in the art in the context of the Specification. *See In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In this case, the phrase "naturally occurring mixture of compounds" does not appear in the Specification as originally filed. However, "naturally occurring" would be understood by persons of skill in the art to mean that it exists or is found in nature – that is, it is "a product of nature" and not "a product of human ingenuity." *Diamond v. Chakrabarty*, 447 US 303, 309, 313 (1980). Thus, we interpret a

"naturally occurring mixture of compounds" to mean a "mixture of compounds" that can be found in nature.

Ethyl 3-mercaptobutyrate was identified by the inventors as a flavorant present in the "complex mixture" of components that naturally occur in mango (Spec. 2: 21-27 and 5: 33 to 6:12). In this context, we interpret "provided that the ethyl 3-mercaptobutyrate is not part of a naturally occurring mixture of compounds" to mean that the mercaptobutyrate compound is not present in the claimed composition in the same complex form in which it would occur in nature.

We have considered, but reject, the Examiner's alternative interpretation (Answer 6-7). As we understand it, the Examiner interprets "naturally occurring mixture of compounds" phrase to mean "a mixture of naturally occurring compounds." In our opinion, the Examiner improperly interpreted "naturally occurring" to describe the compounds present in the mixture, rather than the entire mixture, itself.

The term "ingestible" as recited in claim 7 is also at issue in this proceeding. The Specification states the ethyl 3-mercaptobuyrate is useful for imparting a unique flavor to foodstuffs (Spec. 5: 33-35). It is described as useful "in a wide variety of ingestible vehicles" that include gum, confectionary products, and beverages (Spec. 8: 7-14). The term "ingestible" is also defined in the Specification to mean "all materials and compositions which are used by or which perform a function in the body" (Spec. 6: 17-21). Thus, we interpret the phrases "ingestible composition" and "ingestible vehicle" as recited in claim 7 to mean materials and compositions suitable as foods.

Written description rejection

Claims 7-12 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner contends that the phrase "provided that the ethyl 3-mercaptobutyrate is not part of a naturally occurring mixture of compounds or part of a synthetic mixture of compounds which is the same as the naturally occurring mixture" of compounds is "new matter" to the application because it is not supported in the Specification as originally filed (Answer 13). "[N]owhere in the written description is language reflecting the present form of claim 7 found" (Final Office Action 9).

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required 'to recount his invention in such detail that his future claims can be determined to be encompassed within his original creation.'" *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1330 [65 USPQ2d 1385] (Fed. Cir. 2003) (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1561 [19 USPQ2d 1111] (Fed. Cir. 1991)). While there is no requirement that the claimed invention be described in the identical wording that was used in the Specification, there must be sufficient disclosure to show one of skill in this art that the inventor "invented what is claimed." *See Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1235 (Fed. Cir. 2000).

According to the Specification, Appellants discovered that ethyl 3-mercaptobutyrate "possesses unexpected flavor properties and imparts a unique note to flavors" especially in foodstuffs (Spec. 5: 33-37). It is present among "[a] relatively large number of components . . . identified in

an analysis of [a solvent extract of] mango" (Spec. 5: 37 to 38). Ethyl 3-mercaptobutyrate is stated to be "present at such low concentrations in mango that it cannot be isolated from the fruit in a commercially viable way" (Spec. 6: 10-12). Instead, Appellants describe the chemical synthesis of ethyl 3-mercaptobuyrate in a "purified form, unaccompanied by substances of natural origin present in mango" (Spec. 4: 35 to 5: 2) and shows that it acts as a beneficial flavorant (Spec. 38-39 (Example 2)). Thus, Appellants' invention is the discovery that purified ethyl 3-mercaptobutyrate acts as a flavoring when introduced into foodstuffs.

The written description must be of sufficient detail to show possession of the full scope of the invention. *Pandrol USA LP v. Airboss Railway Products Inc.*, 424 F.3d 1161, 1165, 76 USPQ2d 1524, 1527 (Fed. Cir. 2005). In this case, naturally occurring mixtures are excluded from the claims, but that leaves the claim open to everything else that contains ethyl 3-mercaptobutyrate – including any composition, however modified that it is no longer naturally occurring.[1] In our opinion, such a claim scope is not justified nor drawn to what Appellants invented. The invention described in the Specification is "purified" ethyl 3-mercaptobutyrate "unaccompanied by substances of natural origin present in mango" (Spec. 4: 35 to 5: 2) as a novel flavoring or perfuming agent. This is the only invention described in the Specification. There is no detail in the Specification that shows that Appellants possessed compositions of a different scope, let alone of an intermediate scope to cover mixtures of less complexity than the naturally-

[1] Such compositions would include, for example, less complex compositions derived from naturally-occurring mixtures by fractionation, extraction, and other processing steps.

occurring mixture from which ethyl 3-mercaptobutyrate was originally identified.

Granted, the purified ethyl 3-mercaptobutyrate described in the application is "not a part of a naturally occurring mixture of compounds." However, what Appellants invented is a "purified" compound that, when introduced into a foodstuff, imparts a unique flavor to it. The only disclosure with respect to naturally occurring mixtures is that the concentration of ethyl 3-mercaptobutyrate is too low for it to be isolated from mango (Spec. 6: 10-12). As a consequence, ethyl 3-mercaptobutyrate was chemically synthesized – the form which is characterized in the Specification as "purified." In sum, we agree with the Examiner that claim 7 lacks a written description in the application.

Our decision is consistent with *In re Johnson and Farnham*, 558 F.2d 1008, 194 USPQ 187 (CCPA 1977), a CCPA case which dealt with exclusionary language in a claim that was not present in the application upon which priority was based. In *Johnson*, the applicant was attempting to narrow the scope of a claimed genus of compounds by excluding two species which had been lost in an interference. The Examiner, in a rejection affirmed by the Board of Appeals, asserted that the claims were not entitled to the 1963 filing date of the application because the claimed subject matter was not described in it as required by 35 U.S.C. § 112, first paragraph. The CCPA reversed. "The only inquiry is whether, after exclusion from the original claims of two species specifically disclosed in the 1963 application, the 1963 disclosure satisfies § 112, first paragraph, for the 'limited' genus now claimed." *Johnson*, 558 F.2d at 1017-1018, 194 USPQ at 195.

The CCPA found that it did because its priority application contained "a broad and complete generic disclosure, coupled with extensive examples fully supportive of the limited genus now claimed." *Johnson*, 558 F.2d at 1018, 194 USPQ at 196.

The CCPA distinguished an earlier case, Welstead, in which an applicant sought to exclude subject matter from an originally claimed genus, because in that case the new subgenus was not described in the application nor was there a description of "[its] species thereof amounting in the aggregate to the same thing." *Johnson*, 558 F.2d at 1018, 194 USPQ at 196.

The CCPA concluded:

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of § 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute.

Johnson, 558 F.2d at 1019, 194 USPQ at 196.

In this case, there is no description in the Specification – as there was in *Johnson* – of a genus minus what has been excluded from the claim. The Specification describes only one species – purified ethyl 3-mercaptobutyrate – and no other. There is no detailed description to show that Appellants possessed the invention which is now claimed.

Appellants argue that "[i]t has always been clear that appellant merely wishes to claim ethyl 3-mercaptobutyrate in purified form as an organoleptic agent and not ethyl 3-mercaptobutyrate in a naturally occurring mixture of compounds or part of a synthetic mixture of compounds which is the same

as the naturally occurring mixture of compounds" (Br. 11). However, purified claim ethyl 3-mercaptobutyrate is not what is presently claimed.

Thus, we conclude that the phrase "provided that the ethyl 3-mercaptobutyrate is not part of a naturally occurring mixture of compounds or a part of a synthetic mixture of compounds which is the same as the naturally occurring mixture of compounds" is new matter to the Specification in violation of the written description requirement of 35 U.S.C. § 112, first paragraph. The rejection of claims 7-12 is affirmed.

Indefiniteness rejection under § 112, second paragraph

There are three rejections at issue in this appeal for lack of definiteness under 35 U.S.C. § 112, second paragraph. First, claims 7-12 stand rejected as indefinite because "it is unclear exactly what constitutes, in the context of the invention, 'a naturally occurring mixture of compounds.'" (Answer 7.) Related to this issue, the Examiner states that if the claims are interpreted to exclude any mixture of naturally occurring compounds, "the compositions specified in claims 10-12 lack antecedent basis" because they would exclude Appellants' "most preferred embodiments: the beverage, confection and chewing gum" (Answer 9-10). Third, the Examiner states that claim 7 is indefinite "[b]ecause a naturally occurring mixture and a synthetic mixture are *not* the same, they cannot as a matter of fact properly be characterized as such" (Answer 13).

We reverse the rejections. The phrase "naturally occurring mixture of compounds," when properly interpreted, means a "mixture of compounds" that can be found in nature (see *supra* at p. 3-4). This is not indefinite nor does it lead claims 10-12 to lack antecedent basis.

The characterization of the synthetic mixture as being the "same" as the naturally occurring mixture would be understood by persons of skill in the art to mean that the profile of compounds in the mixtures are the same. Thus, we do not find that this term introduced ambiguity into the claim.

Anticipation by Nielsen

Claims 7-9 stand rejected under 35 U.S.C. § 102 as anticipated by Nielsen.

Nielsen describes the synthesis of ethyl 3-mercaptobutyrate (Nielsen, at 408; Answer 11). The ethyl 3-mercaptobutyrate accumulates in a hexane phase in the reaction vessel (Nielson, at 408; Answer 11). The Examiner contends that "[s]ince hexane is an ingestible vehicle, in the broadest reasonable interpretation of the term, when considered in light of the instant specification, the Nielsen . . . reference is anticipatory. Hexane is capable of being ingested, thus it is an ingestible material" (Answer 11).

Appellants contend that hexane is not an "ingestible vehicle" as would be understood in the light of the Specification (Br. 7-8). "As set out in appellant's specification, 'ingestible' means to take in as food. Appellant's specification states that '[a]pplicant has discovered that ethyl 3-mercaptobutyrate . . . possesses unexpected flavor properties and imparts a unique note to flavors, *especially for conferring in foodstuffs* . . .' Appellant's specification at page 5, lines 27-31. (emphasis added)" (Br. 8). Appellants provide evidence that hexane is "a toxic substance causing central nervous system effects including dizziness, giddiness, nausea, and headache" and therefore not ingestible as a food (Br. 7-8).

In our opinion, Appellants have the better argument. Claim terms are given their broadest reasonable interpretation as they would be understood by persons of ordinary skill in the art when read in the context of the Specification. We have interpreted "ingestible" to mean a material that can be present in a food (see *supra* at p. 4) because the Specification describes the invention as purified ethyl 3-mercaptobutyrate as a flavoring to be used in foodstuffs (Spec. 5: 33-38). The Examiner's interpretation of "ingestible vehicle" is broad, but not *reasonable* in light of the Specification's teaching about the use of ethyl 3-mercaptobutyrate in food.

Appellants have introduced evidence, unrebutted by the Examiner, that hexane is a toxic substance and therefore would not be considered an "ingestible vehicle" as required by claim 7. We find this evidence persuasive, and thus concur with Appellants that the Examiner erred in rejecting claims 7-9 as anticipated by Nielsen. We reverse this rejection.

Anticipation by Lazier

Claim 7 stands rejected under 35 U.S.C. § 102(b) as anticipated by Lazier.

Lazier teaches the synthesis of ethyl 3-mercaptobutyrate having 87% purity (Lazier, at col. 3, ll. 35-37; Answer 12). The Examiner contends that this composition meets the limitation of claim 7 requiring the presence of an ingestible vehicle "because there is some additional material contained besides the mercapto-ester compound (the 'ingestible vehicle')" (Answer 12).

Appellants contend that "[t]he Examiner may NOT assume that this additional material (13%) is an ingestible material. Lazier et al. does not

identify this additional material. This additional material could just as readily be one or more toxic (non-food) substances. Lazier et al. was not seeking to make flavoring agents for use in ingestible vehicles but rather was seeking to make starting materials for use in polymers (Lazier et al. at col. 1, lines 4-9). Hence, Lazier et al. was not concerned whether this additional material (13%) was an ingestible material" (Br. 10).

"A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the claimed invention. Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1667 (Fed. Cir. 2003) (internal citations omitted). *See* also *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F3d 1331, 1343 74 USPQ2d 1398, 1406 (Fed. Cir. 2005). "[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

The issue raised by this rejection is whether the Examiner has provided a reasonable basis for shifting the burden to Appellants to establish that the claimed composition is distinguishable from Lazier's composition; and if so, whether Appellants' burden has been met. In our opinion, the Examiner met his burden, but Appellants did not.

Lazier's Example II, relied upon by the Examiner for its disclosure of a fraction that "analyzes for 87% purity as ethyl 3-mercaptobutyrate" (Lazier, at col. 3, ll. 36-38), also comprises "[w]ater . . . formed in the course

of the reaction" (Lazier, at col. 3, ll. 38-39). Since water is an ingestible vehicle, we conclude that its presence is enough to provide reasonable basis for considering Lazier's composition to be the same as the composition of claim 7. Appellants had the opportunity to provide evidence that Lazier's synthetic method would not result in an ingestible composition as required by claim 7, but no evidence was offered in rebuttal. Accordingly, we affirm the rejection.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Ssc

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